04-17-06

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(to be used for all correspondence after initial filing)

Application Number	10/804,679
Filing Date	March 18, 2004
First Named Inventor	Andrew D. SUTTON
Art Unit	1616
Examiner Name	G. Konata
Total Number of Pages in This Submission: 19	Attorney Docket Number: 263742002802

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Firm Name	MORRISON & FOERSTER LLP (Customer No. 25226)		
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Date	April 14, 2006	Reg. No.	43,318

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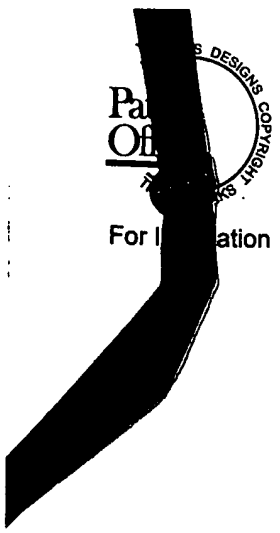

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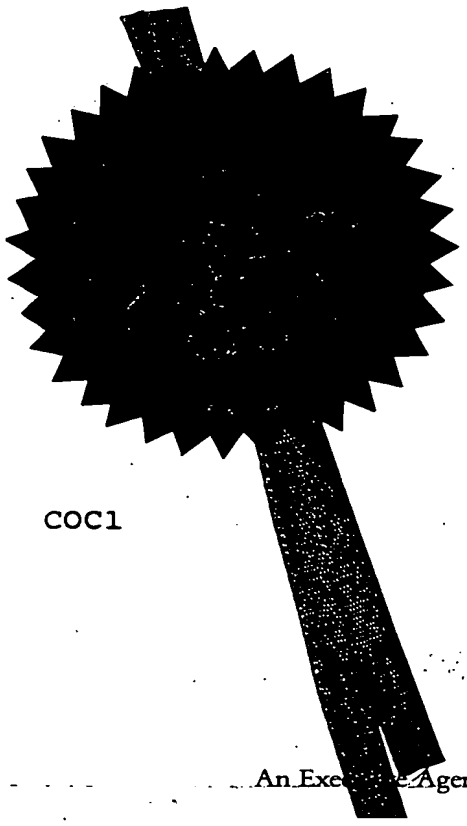

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Patents Act 1977

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1 Please give the title of the invention

PREPARATION OF DIAGNOSTIC AGENTS

❷ Applicant's details

❑ **First or only applicant**

2a If you are applying as a corporate body please give:

Corporate name

MOONBROOK LIMITED

Country *(and State of incorporation, if appropriate)* UNITED KINGDOM

2b If you are applying as an individual or one of a partnership please give in full:

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Forenames

2c **In all cases**, please give the following details:

Address 137 HIGH STREET
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UK postcode *(if applicable)* DE14 1JZ

Country UNITED KINGDOM

ADP number *(if known)* 5869342001

2d, 2e and 2f: If there are further applicants please provide details on a separate sheet of paper.

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Yes [x] No [ ] ➡ ***go to 3b***

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Agent's name ERIC POTTER & CLARKSON

Agent's address ST MARY'S COURT
ST MARY'S GATE
NOTTINGHAM

Postcode NG1 1LE

Agent's ADP number 1305010

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❺ Claiming an earlier application date

5 Are you claiming that this application be treated as having been filed on the date of filing of an earlier application?

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Yes ☐ No ☒ ➡ ***go to 6***

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Continuation sheets for this Patents Form 1/77			
Claim(s)	2	Description	22
Abstract	1	Drawing(s)	1

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PREPARATION OF DIAGNOSTIC AGENTS

The present invention relates to the preparation of diagnostic agents comprising hollow proteinaceous microcapsules used to enhance ultrasound imaging.

The fact that air bubbles in the body can be used for echocardiography has been known for some time. Bubble-containing liquids can be injected into the bloodstream for this purpose (see Ophir *et al* (1980) "Ultrasonic Imaging" 2, 67-77, who stabilised bubbles in a collagen membrane) and EP-A-224934 and EP-A-324938 disclose the use of bubbles prepared by sonicating an albumin solution. However, the size distribution of the bubbles is apparently uncontrollable and the bubbles disappear when subjected to pressure experienced in the left ventricle (Shapiro *et al* (1990) *J. Am. Coll. Cardiology*, 16(7), 1603-1607.

EP-A-52575 discloses, for the same purpose, solid particles which have gas entrained in them, the gas being released from the particles in the bloodstream.

We have now found that a process of spray-drying a solution of microcapsule-forming agent and then insolubilising the microcapsules which are formed leads to an improved product. Przyborowski *et al* (1982 *Eur. J.*

Nucl. Med. 7, 71-72) disclosed the preparation of human serum albumin (HSA) microspheres by spray-drying for radiolabelling and subsequent use in scintigraphic imaging of the lung. The microspheres were not said to be hollow and, in our repetition of the work, only solid microspheres are produced. Unless the particles are hollow, they are unsuitable for echocardiography. Furthermore, the microspheres were prepared in a one step process which we have found to be unsuitable for preparing microcapsules suitable for echocardiography; it was necessary to remove undenatured albumin from the microspheres (which is not necessary in our process); and a wide size range of microspheres was apparently obtained, as a further sieving step was necessary. Hence, not only was the Przyborowski *et al* process not an obvious one to choose for the preparation of microcapsules useful in ultrasonic imaging but the particles produced were unsuitable for that purpose and, by adapting it, we have devised a considerable improvement over that prior process.

The Przyborowski *et al* article refers to two earlier disclosures of methods of obtaining albumin particles for lung scintigraphy. Aldrich & Johnston (1974) *Int. J. Appl. Rad. Isot.* 25, 15-18 disclosed the use of a spinning disc to generate 3-70 μm diameter particles

which are then denatured in hot oil. The oil is removed and the particles labelled with radioisotopes. Raju *et al* (1978) *Isotopenpraxis* 14(2), 57-61 used the same spinning disc technique but denatured the albumin by simply heating the particles. In neither case were hollow microcapsules mentioned and the particles prepared were not suitable for echocardiography.

One aspect of the present invention provides a process comprising the steps of (i) spray-drying a solution or dispersion of a wall-forming material in order to obtain intermediate microcapsules and (ii) reducing the water-solubility of at least the outside of the intermediate microcapsules.

The two steps of the process may be carried out as a single process or the intermediate product of step (i) may be collected and separately treated in step (ii). These two possibilities are referred to hereinafter as the one step and two step processes.

The wall-forming material and process conditions should be so chosen that the product of step (ii) is non-toxic and non-immunogenic in the conditions of use, which will clearly depend on the dose administered and duration of treatment. The wall-forming material may be a starch

derivative or a polysaccharide such as polydextrose. Preferably, the wall-forming material is a protein such as collagen, gelatin or (serum) albumin, in each case preferably of human origin (ie derived from humans or corresponding in structure to the human protein). Most preferably, it is human serum albumin (HA) derived from blood donations or, ideally, from the fermentation of microorganisms (including cell lines) which have been transformed or transfected to express HA.

Techniques for expressing HA (which term includes analogues and fragments of human albumin, for example those of EP-A-322094, and polymers of monomeric albumin) are disclosed in, for example, EP-A-201239 and EP-A-286424. All references are included herein by reference. "Analogues and fragments" of HA include all polypeptides (i) which are capable of forming a microcapsule in the process of the invention and (ii) of which a continuous region of at least 50% (preferably at least 75%, 80%, 90% or 95%) of the amino acid sequence is at least 80% homologous (preferably at least 90%, 95% or 99% homologous) with a continuous region of at least 50% (preferably 75%, 80%, 90% or 95%) of human albumin.

In the following description of preferred embodiments, the term "protein" is used since this is what we prefer but it is to be understood that other biocompatible wall-forming materials can be used.

The protein solution or dispersion is preferably 0.1 to 50% w/v, more preferably about 5.0 - 25.0% protein, particularly when the protein is albumin. About 20% is typical. Mixtures of proteins may be used, in which case the percentages in the last sentence refer to the total protein content, and non-proteinaceous components may be present.

The protein solution or dispersion (preferably solution), referred to hereinafter as the "protein preparation", is spray-dried by any suitable technique which results in discrete microcapsules of 0.01 - 50.0 μm diameter. These figures refer to at least 90% of the population of microcapsules and the diameter is measured by microscopic image analysis. The term "microcapsules" means hollow particles enclosing a space, which space is filled with a gas or vapour but not with any solid materials. Honeycombed particles resembling the confectionery sold in the UK as "Maltesers" (Regd TM) are not formed. It is not necessary for the space to be totally enclosed (although this is preferred) and it is not necessary for

the microcapsules to be precisely spherical, although they are generally spherical. If the microcapsules are not spherical, then the diameters referred to above relate to the diameter of a corresponding spherical microcapsule having the same mass and enclosing the same volume of hollow space as the non-spherical microcapsule.

The spray-drying comprises forming an aerosol of the protein preparation by, for example, forcing the preparation through at least one orifice under pressure or by using a centrifugal atomizer, into a chamber of warm air or other inert gas. The chamber should be big enough for the largest ejected drops not to strike the walls. The gas or vapour in the chamber is clean (ie preferably sterile and pyrogen-free) and non-toxic when administered into the bloodstream in the amounts concomitant with administration of the micro-capsules in echocardiography. The rate of evaporation of the liquid from the protein preparation should be sufficiently high to form hollow microcapsules but not so high as to burst the microcapsules. The rate of evaporation may be controlled by varying the gas flow rate, concentration of protein in the protein preparation, nature of liquid carrier and, most importantly, the temperature of the gas encountered by the aerosol. With an albumin concentration of 15-25% in water, an inlet gas

temperature of at least about 100°C, preferably at least 110°C, is generally sufficient to ensure hollowness and may be as high as 200-250°C without the capsules bursting. The temperature may, in the one step version of the process of the invention, be sufficient to insolubilise the wall-forming material. Since the temperature of the gas encountered by the aerosol will depend also on the rate at which the aerosol is delivered and on the liquid content of the protein preparation, the outlet temperature may be monitored to ensure an adequate temperature in the chamber. An outlet temperature of 40 - 150°C has been found to be suitable.

In the two step process, the intermediate microcapsules comprise typically 96 - 98% monomeric HA and have a limited *in vivo* life time for ultrasound imaging. They may, however, be stored and transported before the second step of the two step process is carried out.

In step (ii) of the process, the intermediate microcapsules prepared by spray-drying are rendered less water-soluble so that they persist for sufficient time to allow ultrasound image enhancement whilst not being so insoluble and inert that they are not biodegradable. This step also strengthens the microcapsules so that they are able to withstand the rigours of administration,

vascular shear and ventricular pressure. Otherwise, the microcapsules burst, which makes the capsules or bubbles less echogenic. Step (ii) of the process may employ heat (for example microwave heat), ionising irradiation (with, for example, a 0.5 - 10.0 MRad dose of gamma rays) or chemical cross-linking using, for example, formaldehyde, glutaraldehyde, ethylene oxide or other agents for cross-linking proteins and is carried out on the substantially dry intermediate microcapsules formed in step (i), or on a suspension of such microcapsules in a liquid in which the microcapsules are insoluble, for example a suitable solvent. In the one step version of the process, a cross-linking agent such as glutaraldehyde may be sprayed into the spray-drying chamber or may be introduced into the protein preparation just upstream of the spraying means. Alternatively, the temperature in the chamber may be high enough to insolubilise the microcapsules. The proportion of the protein which has been rendered insoluble is measured by gel permeation HPLC or gel electrophoresis.

The final product, measured in the same way as the intermediate microcapsules, preferably consists of microcapsules having a diameter of 0.05 to 50.0 μm, more preferably 0.1 to 20.0 μm and especially 1.0 to 8.0 μm. We have found that a range of about 0.5 to 3.0 μm is

especially suitable for the production of a low contrast image and for use in colour Doppler imaging, whereas a range of about 4.0 to 6.0 μm is better for the production of sharp images. One needs to take into account the fact that step (ii) may alter the size of the microcapsules in determining the size produced in step (ii).

We have used the process described above to prepare novel hollow microspheres useful in diagnostic imaging. The walls of the microcapsules are 40-500 nm thick (ie that is the difference between the outer and inner diameters), which distinguishes them from the sonicated microbubbles of EP-A-224 934 and EP-A-324 938, which have much thinner walls.

Thus, a further aspect of the invention provides hollow microcapsules having walls 40-500 nm thick, preferably 100-500 nm, preferably formed of protein as described above.

The product is generally supplied and stored as a dry powder and is suspended in a suitable sterile, non-pyrogenic liquid just before administration. The suspension is generally administered by injection of about 1.0-10.0 ml into a suitable vein such as the cubital vein or other bloodvessel. A microcapsule

concentration of about 1.0×10^5 to 1.0×10^9 particles/ml is suitable, preferably about 5.0×10^5 to 5.0×10^7.

Although ultrasonic imaging is applicable to various animal and human body organ systems, one of its main applications is in obtaining images of myocardial tissue and perfusion or blood flow patterns.

The techniques use ultrasonic scanning equipment consisting of a scanner and imaging apparatus. The equipment produces visual images of a predetermined area, in this case the heart region of a human body. Typically, the transducer is placed directly on the skin over the area to be imaged. The scanner houses various electronic components including ultrasonic transducers. The transducer produces ultrasonic waves which perform a sector scan of the heart region. The ultrasonic waves are reflected by the various portions of the heart region and are received by the receiving transducer and processed in accordance with pulse-echo methods known in the art. After processing, signals are sent to the imaging apparatus (also well known in the art) for viewing.

In the method of the present invention, after the patient is "prepped" and the scanner is in place, the microcapsule suspension is injected, for example through an arm vein. The contrast agent flows through the vein to the right venous side of the heart, through the main pulmonary artery leading to the lungs, across the lungs, through the capillaries, into the pulmonary vein and finally into the left atrium and the left ventricular cavity of the heart.

With the microcapsules of this invention, observations and diagnoses can be made with respect to the amount of time required for the blood to pass through the lungs, blood flow patterns, the size of the left atrium, the competence of the mitral valve (which separates the left atrium and left ventricle), chamber dimensions in the left ventricular cavity and wall motion abnormalities. Upon ejection of the contrast agent from the left ventricle, the competence of the aortic valve also may be analyzed, as well as the ejection fraction or percentage of volume ejected from the left ventricle. Finally, the contrast patterns in the tissue will indicate which areas, if any, are not being adequately perfused.

In summary, such a pattern of images will help diagnose unusual blood flow characteristics within the heart, valvular competence, chamber sizes and wall motion, and will provide a potential indicator of myocardial perfusion.

The microcapsules permit left heart imaging from intravenous injections. The albumin microcapsules, when injected into a peripheral vein, are capable of transpulmonary passage. This results in echocardiographic opacification of the left ventricle (LV) cavity as well as myocardial tissue.

Besides the scanner briefly described above, there exist other ultrasonic scanners, examples of which are disclosed in US Patents Nos. 4,134,554 and 4,315,435, the disclosures of which are herein incorporated by reference. Basically, these patents relate to various techniques including dynamic cross-sectional echography (DCE) for producing sequential two-dimensional images of cross-sectional slices of animal or human anatomy by means of ultrasound energy at a frame rate sufficient to enable dynamic visualisation of moving organs. Types of apparatus utilised in DCE are generally called DCE scanners and transmit and receive short, sonic pulses in the form of narrow beams or lines. The reflected

signals' strength is a function of time, which is converted to a position using a nominal sound speed, and is displayed on a cathode ray tube or other suitable devices in a manner somewhat analogous to radar or sonar displays. While DCE can be used to produce images of many organ systems including the liver, gall bladder, pancreas and kidney, it is frequently used for visualisation of tissue and major blood vessels of the heart.

The microcapsules may be used for imaging a wide variety of areas, even when injected at a peripheral venous site. Those areas include (without limitation): (1) the venous drainage system to the heart; (2) the myocardial tissue and perfusion characteristics during an exercise treadmill test or the like; and (3) myocardial tissue after an oral ingestion or intravenous injection of drugs designed to increase blood flow to the tissue. Additionally, the microcapsules may be useful in delineating changes in the myocardial tissue perfusion due to interventions such as (1) coronary artery vein grafting; (2) coronary artery angioplasty (balloon dilation of a narrowed artery); (3) use of thrombolytic agents (such as streptokinase) to dissolve clots in coronary arteries; or (4) perfusion defects or changes due to a recent heart attack.

Furthermore; at the time of a coronary angiogram (or a digital subtraction angiogram) an injection of the microcapsules may provide data with respect to tissue perfusion characteristics that would augment and complement the data obtained from the angiogram procedure, which identifies only the anatomy of the blood vessels.

Through the use of the microcapsules of the present invention, other non-cardiac organ systems including the liver, spleen and kidney that are presently imaged by ultrasonic techniques may be suitable for enhancement of such currently obtainable images, and/or the generation of new images showing perfusion and flow characteristics that had not previously been susceptible to imaging using prior art ultrasonic imaging techniques.

Preferred aspects of the present invention will now be described by way of example and with reference to Figure 1, which is a partly cut away perspective view from the front and one side of suitable spray-drying apparatus for the first stage of the process of the invention.

EXAMPLE 1

A suitable spray dryer (Figure 1) is available from A/S Niro Atomizer, Soeborg, Denmark under the trade designation "Mobile Minor". It comprises a centrifugal atomizer (Type M-02/B Minor), driven by an air turbine at an air pressure of min 4 bar and up to max 6 bar. At 6 bar an atomizer wheel speed of approx 33,000 rpm is reached. Turning on and off the compressed air to the atomizer is done by means of a valve placed in the instrument panel. The maximum consumption of compressed air to the atomizer is 17 Nm^3/h at a pressure of 6 bar. All parts coming into contact with the liquid feed and powder are made of stainless steel AISI 316, except for the pump feed tube and the atomizer wheel, which is made of stainless steel AISI 329, made to resist high centrifugal force.

The drying chamber has an inside made of stainless steel AISI 316, well insulated with Rockwool, and covered outside with a mild steel sheeting. The drying chamber is provided with a side light and observation pane for inspection during the operation. The roof of the drying chamber is made inside of stainless steel AISI 316 and outside of stainless steel AISI 304.

An air disperser made of stainless steel AISI 304, is used for distribution of the air in the drying chamber in order to achieve the best possible drying effect. An air duct, made of stainless steel AISI 316, provides lateral transportation of the exhaust air and the powder to the cyclone, which is made of stainless steel AISI 316 and designed to separate the powder and air.

A closing valve of the butterfly valve type, also made of stainless steel AISI 316 and having a gasket of silicone rubber, is used for powder discharge under the cyclone into a powder collecting glass jar tightly placed under the cyclone by means of a spring device.

A fan made of silumin, complete with 3-phase squirrel-cage motor, 0.25 kW, and V-belt drive with belt-guard, draws air and powder through the drying chamber and cyclone.

An air heater heats the drying air by means of electricity (total consumption 7.5 kWh/h, infinitely variable) and can give inlet air temperatures of up to about 350°C, although this is generally too high for preparing the microcapsules of the invention.

Equipment for two-fluid nozzle atomization may be added, which is made of stainless steel AISI 316, consisting of entrance pipe with nozzle holder and nozzle, to be placed in the ceiling of the drying chamber. The equipment includes an oil/water separator, reduction valve and pressure gauge for compressed air to the two-fluid nozzle. Consumption of compressed air: 8-15 kg/h at a pressure of 0.5-2.0 bar.

A suitable feed pump for transport of feed to the atomizer device is a peristaltic pump. The pump is provided with a motor (1 x 220V, 50 Hz, 0.18 kW) and a continuously variable gear for manual adjustment. A feed pipe made of silicone hose leads from a feed tank (local supply) through the feed pump to the atomization device.

An absolute air filter, consisting prefilter, filter body in stainless steel and absolute air filter, is used for the treatment of the ingoing drying air to render it completely clean.

A 20% solution of sterile, pyrogen-free rHA in pyrogen-free water (suitable for injection) was pumped to the nozzle of a two fluid nozzle atomiser mounted in the commercial spray drying unit described above. The peristaltic pump speed was maintained at a rate of

approximately 10 ml/minute such that with an inlet air temperature of 190°C the outlet air temperature was sustained at 105°C.

Compressed air was supplied to the two fluid atomising nozzle at 1.0-5.0 Bar. In this range microcapsules of size 0.1-8.0 µm are obtained.

The first few grams of material were not collected. The bulk of the material was gathered from the collection vessel underneath the cyclone, in preparation for the second step of insolubilisation.

In step (ii) of the process, a small aliquot of the microcapsules (0.5 g) was heated in a microwave oven such that it received 125-150 watt hours of microwave heat at 2500 mHz. This yielded microcapsules in which 10-20% of the rHA was insoluble (as determined by GPC) and as a result of this heat fixation their *in vitro* echogenic half-life increased from 1-2 minutes to 30 minutes.

EXAMPLE 2

The process of Example 1 was repeated but with the following differences in step (i): a centrifugal atomiser was used instead of a two fluid nozzle; the

inlet temperature was 150°C (with the outlet air temperature still being sustained at 105°C); and compressed air was supplied to the nozzle at 1.0-6.0 Bar. The wheel rotated at 20-40,000 rpm and delivered droplets, and subsequently microcapsules, in the 1.0-8.0 μm range.

EXAMPLE 3

Step (ii) of the process of Example 1 or 2 was varied as follows. A small aliquot of the microcapsules (0.5 g) was heated in a microwave oven such that it received 300-350 watt hours of microwave heat at 2500 mHz. This yielded microcapsules in which 90-95% of the monomeric rHA was insoluble (as determined by GPC) and as a result of this heat fixation their *in vitro* echogenic half-life increased from 1-2 minutes to in excess of one hour.

EXAMPLE 4

Step (ii) of the process of Example 1 or 2 was varied as follows. A small aliquot of the microcapsules (0.5 g) was sealed under argon in a glass vial. The vial was cooled to 4°C and then irradiated with a ^{60}Co gamma radiation source to deliver a 0.5 MRad dose of gamma rays. The irradiation resulted in the formation of

microcapsules in which 10-15% of the monomeric albumin was insoluble. This extended the *in vitro* echogenic half-life of the microcapsules from 1-2 minutes to approximately 30 minutes.

EXAMPLE 5

Step (ii) of the process of Example 1 or 2 was varied as follows. A small aliquot of the microcapsules (0.5 g) was sealed under argon in a glass vial. The vial was cooled to 4°C and then irradiated with a ^{60}Co gamma radiation source to deliver a 7.5 MRad dose of gamma rays to the microcapsules. The irradiation resulted in the formation of microcapsules in which 60-70% of the monomeric rHA was insoluble, thereby extending their echogenic half-life from 1-2 minutes to a minimum of 60 minutes.

EXAMPLE 6

Step (ii) of the process of Example 1 or 2 was varied as follows.

A small aliquot of microcapsules (0.5 g) was resuspended in 5 ml of ethanol, chloroform or methylene chloride containing a) 1.5% glutaraldehyde, b) 2.0% diphthaloyl

chloride or c) 5.0% formaldehyde. The microcapsules were stirred for varying times from 10 minutes to 3 hours. The microcapsules were removed by filtration and washed thoroughly in the original organic buffer containing 5% ethanolamine, in order to remove excess cross-linking agent. Finally the microcapsules were washed in organic solvent and vacuum dried to remove any residual solvents. The extent of insolubilisation may be varied from 5-100% by this method resulting in the extension of *in vitro* echogenic half-life from 1-2 minutes to in excess of one hour.

EXAMPLE 7

The two independent steps of microcapsule formation and insolubilisation of the shell may be combined in a single process. The formation of the microcapsules and the insolubilisation of the polymeric material are achieved simultaneously during the spray drying process.

A solution of rHA was fed by peristaltic pump to a small reaction chamber, with a separate feed line supplying a 5% solution of a suitable crosslinking agent, eg glutaraldehyde, diphthaloyl chloride or formaldehyde. The residence time in the reaction chamber was such that initial adduct formation between the crosslinking agent

and the protein is achieved, but intraprotein crosslinking is prevented. The reaction vessel outlet was fed directly to the two fluid nozzle atomisers mounted in a specially adapted spray drying unit, capable of handling volatile solvents. The conditions of spray drying were as outlined in Example 1. The microcapsules were incubated dry at room temperature to allow intraprotein crosslinks to form and then suspended in ethanol containing 5% ethanolamine to quench any remaining crosslinking agent. Thorough washing of the microcapsules was performed and finally the microcapsules were vacuum dried to remove residual solvent.

CLAIMS

1. Hollow microcapsules having walls 40-500 nm thick and an external diameter of 0.01-50.0 μm.

2. A process comprising the steps of (i) spraying a solution or dispersion of a wall-forming material in a liquid carrier into a gas in order to obtain hollow intermediate microcapsules by evaporation of the liquid carrier and (ii) reducing the water-solubility of at least the outside of the intermediate microcapsules.

3. A process according to Claim 2 wherein the wall-forming material is a protein.

4. A process according to Claim 3 wherein the protein is collagen, gelatin or serum albumin.

5. A process according to Claim 3 or 4 wherein the protein solution or dispersion comprises 10.0 - 25.0% protein.

6. A process according to any one of Claims 3 to 5 wherein in step (i) the protein solution or dispersion is spray-dried to form discrete microcapsules of 0.01 - 50.0 μm diameter.

7. A process according to any one of Claims 3 to 6 wherein the product of step (i) comprises 96 - 98% monomeric protein.

8. A process according to any one of Claims 2 to 6 wherein the conditions of step (i) are such as to achieve step (ii) also.

9. Microcapsules obtained by a process according to any one of Claims 2 to 8.

10. Microcapsules obtainable by a process according to any one of Claims 2 to 8.

11. A method of generating an image for subsequent inspection, comprising (a) injecting into the body of a mammal microcapsules according to any one of Claims 1, 9 or 10, (b) subjecting the mammal or part thereof to suitable ultrasonic radiation and (c) detecting ultrasonic radiation reflected, transmitted, resonated or frequency modulated by the said microcapsules.

12. Any novel feature or combination of features disclosed herein.

ABSTRACT

Preparation of Diagnostic Agents

Microcapsules are prepared by a process comprising the steps of (i) spray-drying a solution or dispersion of a wall-forming material in order to obtain intermediate microcapsules and (ii) reducing the water-solubility of at least the outside of the intermediate microcapsules.

Suitable wall-forming materials include proteins such as albumin and gelatin.

The microcapsules have walls of 40-500 nm thick and are useful in ultrasonic imaging.

Principal Features of the Mobile Minor Spray Dryer

– **Feeding device.**

– **[redacted]ng air disperser** ensures effective [redacted]ol of the air flow pattern. Swirling air is directed around the vaned disc atomizer.

C – **Rotary atomizer** or nozzle atomizer.

D – The stainless steel **interconnecting pipe** system can easily be stripped down for cleaning.

E – **Steps** for access to the chamber top.

F – **Air valve** for activation of the pneumatic lifting device when raising the chamber lid.

G – **Rubber castors** for unit mobility.

H – **The powder and the exhausted drying air** are separated in a highly-efficient stainless steel cyclone.

I – The powder is recovered in a glass jar.

K – **Instrument panel** centrally located.

L – **Centrifugal exhaust fan** with 3-phase motor.

M – **Damper** for air flow control.

N – **The electric air heater** provides drying air temperatures up to 350° C. The drying air temperature can be continuously adjusted using a percentage timer switch. Max. power consumption 7.5 kW.

Evaporative capacity

Drying Air	Inlet Air Temperature	Outlet Air Temperature	Evaporat Capac:
85 kg/h	150° C	80° C	1.3 kg.
85 kg/h	170° C	85° C	1.7 kg.
80 kg/h	200° C	90° C	2.5 kg.
80 kg/h	240° C	90° C	3.4 kg.
75 kg/h	350° C	90° C	7.0 kg.

Weight and dimension

Weight	280 kgs	620 lbs.
Length	1800 mm	5' 11"
Height	2200 mm	7' 3"
Width	925 mm	3'

Power. The unit can only be operated on a 3-phase power supply (50 or 60 Hz) at alternative voltages of 440, 415, 400, 380, 220, 200 V.

All parts coming into contact with the liquid or the product are made of acid-resistant, stainless steel AISI 316.

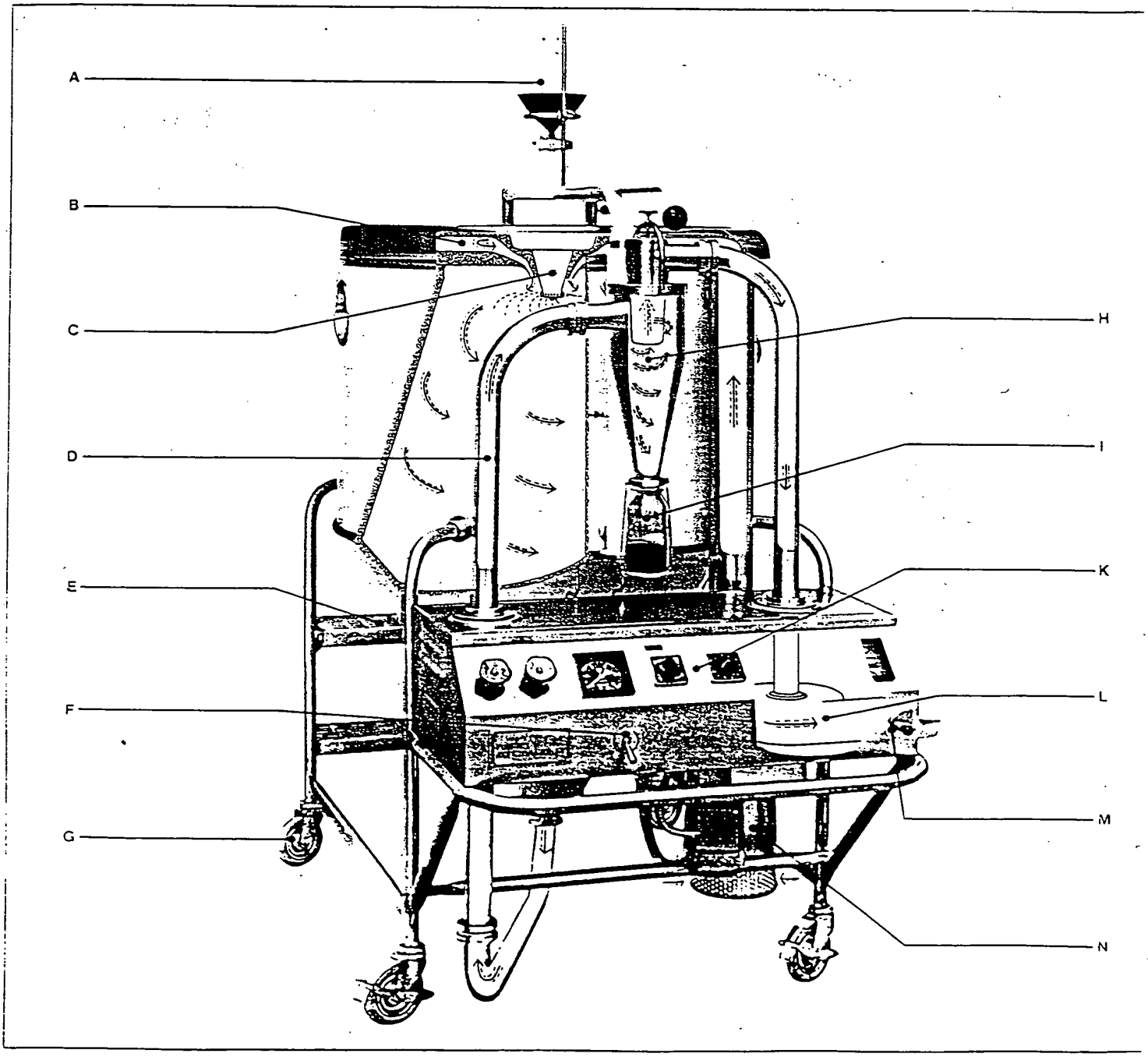

Figure 1